REMARKS

Applicant respectfully requests reconsideration. Claims 1-13, 16-34 and 36-45 were previously pending in this application. By this amendment, Applicant is canceling claims 2-13, 16-34 and 36-45 without prejudice or disclaimer. Claim 1 has been amended. New claims 46-94 have been added. Support for the claim amendment and the new claims can be found in the specification at least on page 1, lines 27-34; page 3, lines 16-18; page 5, lines 11-34; page 6, lines 1-9; page 11, lines 4-5; page 14, lines 4-24; page 16, lines 16-36; page 17, lines 6-35; page 18, lines 1-27; page 20, lines 22-26; page 21, lines 21-27; page 22, lines 7-15; page 23, line 5 through page 24, line 2; page 26, line 17 through page 27 line 2; page 29, lines 22-28; page 38, lines 19-23; page 39, lines 26-27; page 48, lines 11-17; pages 53-57, Table 5; and in claims 3-5, 13, 33, 36 and 38 as originally filed. As a result, claims 1 and 46-94 are pending for examination with claims 1 and 46 being independent claims. No new matter has been added.

Objections to the Claims

Claim 2 is objected to as encompassing non-elected embodiments.
Applicant has canceled claim 2, accordingly this objection is now moot.

Claims 2-9, 44 and 45 are objected to because "A" should have been "The" for said dependent claims. Applicant has canceled claims 2-9, 44 and 45, accordingly this objection is now moot.

Accordingly, reconsideration and withdrawal of this objection is respectfully requested.

Objections to the Drawings

The Examiner objected to the drawing because Figures 1-4 allegedly are missing.

Applicant respectfully traverses. Applicant has submitted a complete copy of the international application on October 12, 2005, including the drawings. Applicant notes that Figures 1-4 are found in the instant application as published on Oct 12, 2006.

Accordingly, reconsideration and withdrawal of this objection is respectfully requested.

Rejections under 35 U.S.C. §112, first paragraph, enablement

The Examiner rejected claims 1, 3-9, 13, 19, 21, 23, 25, 27, 29, 31, 33, 36, and 42-45 under 35 U.S.C. §112, first paragraph, as not enabling. According to the Examiner, while being enabling for an isolated anti-Epidermal Growth factor receptor (EGFR) single domain antibody comprising the amino acid sequence of SEQ ID NO:6, a humanized EGFR single domain antibody comprising the amino acid sequence of SEQ ID NO:13, a composition comprising the EGFR single domain antibody comprising the amino acid sequence of SEQ ID NO: 6 and a carrier for targeting EGFR, a kit comprising the EGFR single domain antibody comprising the amino acid sequence of SEQ ID NO:6 for detecting EGFR polypeptide and the bispecific single domain antibody that binds specifically to EGFR and serum albumin comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 27-40, **does not** reasonably provide enablement for (1) any anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR as set forth in claims 1, and 5-7 for treating and/or preventing and/or alleviating any disorders such as any cancer, rheumatoid arthritis, psoriasis, or hypersecretion of mucus in the lung, (2) any anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR further comprising any single domain antibody directed against any serum protein, (3) anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR further comprising any single domain antibody as set forth in claim 4, (4) any anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR wherein said at least one single domain antibody is any homologous sequence, any functional portion, or any functional portion of any homologous sequence of any full length single domain antibody, (5) any anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR wherein said at least one single domain antibody is any homologous sequence, any functional portion, or any functional portion of any homologous sequence of any full length anti-EGFR polypeptide, (6) any kit comprising any anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR and Epidermal Growth Factor or any fragment thereof, (7) a method for the preparation of a medicament

comprising any anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR and a carrier, (8) any composition comprising any anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR and a suitable pharmaceutical vehicle, (9) any kit comprising any anti-Epidermal Growth Factor Receptor EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR as set forth in claims 36 and 42, and (10) any therapeutic composition comprising any VHH which inhibits the growth of human tumor cells by said VHH binding to Epidermal Growth Factor Receptor of said human tumor cells and (b) any anti-neoplastic agent as set forth in claims 42-45. According to the Examiner, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant respectfully disagrees. Applicant has amended claim 1 to include the limitation "wherein said single domain antibody inhibits and/or blocks the interaction between EGF and EGFR". In addition, Applicant has canceled claims 2-45 and introduced new claims 46-94. The claims now recite: (1) A single domain antibody directed against EGFR, wherein said single domain antibody inhibits and/or blocks the interaction between EGF and EGFR; (2) A single domain antibody directed against EGFR, wherein the sequence is represented by SEQ ID NO:6, or a homologous or functional portion thereof; (3) Anti-EGFR polypeptides essentially consisting of SEQ ID NO;6 and at least one single domain antibody directed against a serum protein; (4) Anti-EGFR polypeptides essentially consisting of SEQ ID NO: 6 and at least one single domain antibody directed against IFN or TNF; (5) Pharmaceutical compositions of the single domain antibodies or anti-EGFR polypeptides; (6) Methods for inhibiting the interaction between EGF and EGFR comprising administering the single domain antibodies or anti-EGFR polypeptides; (7) Kits for screening agents that modulate EGFR-mediated disorders comprising the single domain antibodies or anti-EGFR polypeptides; and (8) Kits for screening for a disorder characterized by dysfunction of EGFR comprising the single domain antibodies or anti-EGFR polypeptides.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988), and include (1) the quantization of experimentation necessary, (2) the amount of direction or guidance presented, (3)

the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability of the art, and (8) the breadth of the claims. Based on a *Wands* factor analysis the Examiner concludes that undue experimentation is required to practice the invention. Respectfully, Applicant requests reconsideration of this conclusion, particularly in view of the amendments made to the claims. Based on these amendments and on Applicant's showing herein as to the state and predictability of the art, Applicant believes Applicant has met the burden of demonstrating that the claims meet the enablement requirement as set forth *In re Wands.*

The Examiner has acknowledged that a single domain antibody directed against EGFR, wherein the sequence is represented by SEQ ID NO: 6 or SEQ ID NO: 13, is enabled. In addition, the Examiner has acknowledged that bispecific single domain antibodies that binds specifically to EGFR and serum albumin comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 27-40 are enabled. In addition to being enabling for a single domain antibody directed against EGFR, wherein the sequence is represented by SEQ ID NO: 6 or SEQ ID NO: 13, and bispecific single domain antibodies that bind specifically to EGFR and serum albumin comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 27-40, the claimed invention is also enabled for single domain antibodies and bispecific domain antibodies with a sequence homologous to SEQ ID NO: 6 and SEQ ID NO: 33, and single domain antibodies wherein the single domain antibody inhibits and/or blocks the interaction between EGF and EGFR.

The specification provides a significant amount of guidance and working examples to the skilled person. The application provides at least 22 examples of EGFR single domain antibodies. In addition, the application teaches additional single domain frameworks. The application has also provided a detailed analysis of the sequence of the claimed single antibodies and a person of ordinary skill in the art can rely on the specification to determine which sequence elements are essential and which sequence elements can be mutated to result in the single domain antibodies of the claimed invention. Furthermore, the application provides an EGFR polypeptide consisting essentially of an anti-EGFR single domain antibody and a single domain antibody against serum albumin. Other single domain antibodies were known in the art at the time of filing (See *e.g.*, PCT/BE03/00193). In addition, Applicant has identified, and provided an assay to identify, single

domain antibodies that inhibit and/or block the interaction between EGF and EGFR (See Example 5 and Table 3).

Thus, based at least on the significant amount of guidance and working examples provided in the application, the knowledge of the person of ordinary skill in the art, and the high level of skill in the art, a person of ordinary skill in the art can practice the claimed invention throughout its reasonable scope without undue experimentation. The skilled person can create additional single domain antibodies and EGFR polypeptides consisting essentially of an anti-EGFR single domain antibody and a single domain antibody against serum proteins without undue experimentation. Thus, Applicant has enabled single domain antibodies, including those with homology to SEQ ID NO: 6 and SEQ ID NO: 33, EGFR polypeptides consisting essentially of an anti-EGFR single domain antibody and a single domain antibody against serum proteins, and single domain antibodies wherein the single domain antibody inhibits and/or blocks the interaction between EGF and EGFR.

The Examiner cites a variety of references in which a single or multiple mutations in the antibody sequence lead to altered specificity or functionality. However, the cited references do not provide a basis for questioning the enablement of the claimed invention. Applicant has provided a detailed sequence analysis of the antibodies of the invention and a person of ordinary skill in the art will know which residues can be mutated without compromising the specificity or functionality of the claimed antibodies. Moreover, it is routine in the art to make and test antibodies with mutations, as is evidenced by the references cited by the Examiner. Thus, any experimentation undertaken by a skilled person is merely routine in the art.

In addition, according to the Examiner, it is unclear what a "functional portion" of a specific antibody is. Applicant has amended the claims and defined a "functional portion" as a "functional portion" that can bind to its target with an affinity of at least 1×10^{-6} M and/or comprising a partial deletion of the complete amino acid sequence while still maintaining the binding sites and protein domains necessary for the binding of and interaction with EGFR. The specification provides working examples for determining if an affinity is at least 1×10^{-6} M and the specification provides a detailed analysis of the amino acids required for binding to and interaction with EGFR. Thus, a person of ordinary skill in the art would understand the meaning of a functional portion and can

produce a "functional portion" of the SEQ ID NO: 6 and SEQ ID NO: 33 without undue experimentation.

Further, according to the Examiner there is no disclosure whether any of the anti-EGFR polypeptides of the invention can treat, much less prevent any disorder relating to any cancer, rheumatoid arthritis, psoriasis, or hypersecretion of mucus in the lung. Although Applicant respectfully disagrees with this assertion of lack of enablement by the Examiner, to facilitate prosecution of the claimed invention, Applicant has canceled without prejudice the claims relating to treatment and prevention of cancer, rheumatoid arthritis, psoriasis, or hypersecretion of mucus in the lung. Accordingly, this part of the rejection is now moot.

Also, according to the Examiner, the term "comprising" is open-ended. Applicant has amended the claims and replaced the term "comprising" with the term "essentially consisting of", thereby limiting the scope of the clamed invention. Accordingly, this part of the rejection is now moot.

Thus, a person of ordinary skill in the art can practice the full scope of the claimed invention by referring to the guidance and working examples of the instant disclosure and utilizing the knowledge in the art, without requiring undue experimentation. Because no undue experimentation is required to practice the claimed invention, the claimed invention is enabled.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. §112, first paragraph, written description

The Examiner rejected claims 1, 3-9, 13, 19, 21, 23, 25, 27, 29, 31, 33, 36, and 42-45 under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification. According to the Examiner, Applicant does not provide written description of (1) any anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR as set forth in claims 1, and 5-7 for treating and/or preventing and/or alleviating any disorders such as any cancer, rheumatoid arthritis, psoriasis, or hypersecretion of mucus in the lung, (2) any anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR further comprising any single domain antibody directed against any serum protein, (3) anti-Epidermal

Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR further comprising any single domain antibody as set forth in claim 4, (4) any anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR wherein said at least one single domain antibody is any homologous sequence, any functional portion, or any functional portion of any homologous sequence of any full length single domain antibody, (5) any anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR wherein said at least one single domain antibody is any homologous sequence, any functional portion, or any functional portion of any homologous sequence of any full length anti-EGFR polypeptide, (6) any kit comprising any anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR and Epidermal Growth Factor or any fragment thereof, (7) a method for the preparation of a medicament comprising any anti-Epidermal Growth Factor Receptor (EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR and a carrier, (8) any composition comprising any anti-Epidermal Growth Factor Receptor EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR and a suitable pharmaceutical vehicle, (9) any kit comprising any anti-Epidermal Growth Factor Receptor EGFR) polypeptide comprising at least any one single domain antibody directed against any EGFR as set forth in claims 36 and 42, and (10) any therapeutic composition comprising any VHH which inhibits the growth of human tumor cells by said VHH binding to Epidermal Growth Factor rRceptor of said human tumor cells and (b) any anti-neoplastic agent as set forth in claims 42-45.

Applicant respectfully disagrees. The written description requirement is satisfied if Applicant can convey with reasonable clarity to a person of ordinary skill in the art that Applicant had possession of the claimed invention at the time of filing. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-1564 (Fed. Cir. 1991). Based on this amendment and on Applicant's showing herein of the support in the specification and the state of the art, Applicant believes Applicant has met the burden of demonstrating that the claims meet the written description requirement.

Applicant has amended the claims and limited the scope of the claimed invention to (1) A single domain antibody directed against EGFR, wherein said single domain antibody inhibits and/or

blocks the interaction between EGF and EGFR; (2) A single domain antibody directed against EGFR, wherein the sequence is represented by SEQ ID NO: 6, or a homologous or functional portion thereof; (3) Anti-EGFR polypeptides essentially consisting of SEQ ID NO: 6 and at least one single domain antibody directed against a serum protein; (4) Anti-EGFR polypeptides essentially consisting of SEQ ID NO: 6 and at least one single domain antibody directed against IFN or TNF; (5) Pharmaceutical compositions of the single domain antibodies or anti-EGFR polypeptides; (6) Methods for inhibiting the interaction between EGF and EGFR comprising administering the single domain antibodies or anti-EGFR polypeptides; (7) Kits for screening agents that modulate EGFR-mediated disorders comprising the single domain antibodies or anti-EGFR polypeptides; (8) Kits for screening for a disorder characterized by dysfunction of EGFR comprising the single domain antibodies or anti-EGFR polypeptides. Applicant has provided an extensive description and a representative number of species for the claimed invention and has thereby shown possession of the claimed invention.

Applicant teaches a representative number of embodiments of single domain antibodies that bind EGFR and a representative number of embodiments of single domain antibodies that inhibit and/or block the interaction between EGF and EGFR. In addition, Applicant teaches that these single domain antibodies can be configured as desired in well-known formats of single domain antibodies by a person of skill in the art. Furthermore, Applicant teaches that single domain antibodies can be raised in *Camelidae*, in addition to those shown in the specification that were raised in *llama.* Also, Applicant teaches serum albumin binding single domain antibodies and combinations with EGFR single domain antibodies to arrive at the claimed anti-EGFR polypeptides. Additional serum protein single domain antibodies were known in the art at the time of filing (See *e.g.*, PCT/BE03/00193), thus a skilled person can readily envision anti-EGFR polypeptides essentially consisting of serum protein single domain antibodies combined with the EGFR single domain antibodies described in the specification. Finally, the court in *Noelle v. Lederman*, 355 F.3d 1343 (Fed. Cir. 2004), when discussing the written description requirement, states "as long as Applicant has disclosed a "fully characterized antigen," either by its structure, formula or chemical name, or physical properties, or by depositing the protein in a public depository, the Applicant can then claim an antibody by its binding affinity to that described antigen." Thus, a person of ordinary

skill in the art can ascertain that Applicant had possession of the claimed invention at the time of filing of the application.

According to the Examiner, the definition of a single domain antibody provided in the specification includes, but is not limited to, heavy chain antibodies, antibodies naturally devoid of light chains, single domain antibodies derived from conventional 4-chain antibodies, engineered antibodies and single domain scaffolds other than those derived from antibodies. Single domain antibodies may be any of the art, or any future single domain antibodies. Single domain antibodies may be derived from any species including, but not limited to mouse, human, camel, llama, goat, rabbit, bovine. However, the passage cited by the Examiner refers to examples of single domain antibodies. The definition of a single chain antibody, as provided in the specification, is "an antibody whose complementary determining regions are part of a single domain polypeptide" (page 13, line 13). Thus, a person of ordinary skill in the art can readily determine if an antibody is a single domain antibody, namely by evaluating if the complementary regions of the antibody are part of a single domain polypeptide. The nature of the antibody, including the species of which the antibody is derived, is not critical as long as the complementary regions are part of a single domain polypeptide.

Also, according to the Examiner, the term "comprising" is open-ended. Applicant has amended the claims and replaced the term "comprising" with the term "essentially consisting of", thereby limiting the scope of the clamed invention. Accordingly, this part of the rejection is now moot.

In addition, according to the Examiner, it is unclear what a "functional portion" of a specific antibody is. Applicant has amended the claims and defined a "functional portion" as a "functional portion" that can bind to its target with an affinity of at least 1×10^{-6} M and/or comprising a partial deletion of the complete amino acid sequence while still maintaining the binding sites and protein domains necessary for the binding of and interaction with EGFR. The specification provides working examples for determining if an affinity is at least 1×10^{-6} M and the specification provides a detailed analysis of the amino acids required for binding to and interaction with EGFR. Thus, a person of ordinary skill in the art would understand the meaning of a functional portion and can

determine that Applicant had possession of a "functional portion" of SEQ ID NO: 6 and SEQ ID NO: 33.

Further, according to the Examiner there is no disclosure whether any of the anti-EGFR polypeptides of the invention can treat, much less prevent any disorder relating to any cancer, rheumatoid arthritis, psoriasis, or hypersecretion of mucus in the lung. Although Applicant respectfully disagrees with this assertion of lack of enablement by the Examiner, to facilitate prosecution of the claimed invention, Applicant has canceled without prejudice the claims relating to treatment and prevention of cancer, rheumatoid arthritis, psoriasis, or hypersecretion of mucus in the lung. Accordingly, this part of the rejection is now moot.

Thus, Applicant shows possession of the claimed invention, and Applicant thereby satisfies the written description requirement.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Rejections under 35 U.S.C. §112, second paragraph,

The Examiner rejected claims 8-9 under 35 U.S.C. §112, second paragraph, as being indefinite. According to the Examiner, the metes and bounds of the term "functional portion" is unclear.

Applicant respectfully disagrees. Applicant has amended the claims and defined a "functional portion" as a "functional portion" that can bind to its target with an affinity of at least 1 x 10^{-6} M and/or comprising a partial deletion of the complete amino acid sequence while still maintaining the binding sites and protein domains necessary for the binding of and interaction with EGFR. The specification provides working examples for determining if an affinity is at least 1 x 10^{-6} M and the specification provides a detailed analysis of the amino acids required for binding to and interaction with EGFR. Thus, a person of ordinary skill in the art would understand the meaning of a "functional portion".

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. §102

The Examiner rejected claims 1, 5, 8-9, 19, 21, 23, 25, 27, 29, 31 and 33 under 35 U.S.C. §102(b) as being anticipated by U.S. Application No. 2002/0058033. According to the Examiner, US 2002/0058033 teaches a single-chain antibody clone (scFv) comprising at least one variable domain from heavy chain directed against EGFR linked to a variable domain from light chain directed against EGFR.

Applicant respectfully traverses. US 2002/0058033 does not teach all the elements of the claimed invention. US 2002/0058033 teaches multiple domain antibodies (*i.e.*, single *chain* antibodies comprising both a heavy chain domain *and* a light chain domain) and does not disclose single *domain* antibodies.

Applicant has amended claim 1 and canceled claims 5, 8-9, 19, 21, 23, 25, 27, 29, 31 and 33. In addition, Applicant has introduced new claims 46-94. The claimed invention pertains to single domain antibodies and anti-EGFR polypeptides *consisting essentially of* single domain antibodies, and compositions, methods and kits comprising these single domain antibodies and anti-EGFR polypeptides. Single domain antibodies are defined on page 13, line 13 of the specification as "antibodies whose complementary determining regions are part of a single domain polypeptide". Thus, the single domain antibodies of the claimed invention contain only *one* antibody binding domain (*e.g.*, the variable domain heavy chain). The single *domain* antibodies of the claimed invention should be distinguished over single *chain* antibodies that contain multiple antibody binding domains (*e.g.*, VH and VL). While the single domain antibodies of the claimed invention may be derived from regular 4-chain antibodies and may be derived from a variety of species, the single domain antibodies are limited to antibodies whose complementary determining regions are part of a single domain polypeptide.

Because US 2002/0058033 does not teach all the elements of the claimed invention, US 2002/0058033 does not anticipate the claimed invention.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

The Examiner rejected claims 1, 5, 13, 36 and 42 under 35 U.S.C. §102(b) as being anticipated by WO 96/34096. According to the Examiner, WO 96/34096 teaches an anti-EGFR

polypeptide such as an Fv antibody fragment from fully-human antibody that binds specifically to EGFR comprising at least one antibody from light chain linked to one antibody domain from heavy chain directed against EGFR.

Applicant respectfully traverses. WO 96/34096 does not teach all the elements of the claimed invention. The single domain antibodies of the claimed invention contain only one antibody binding domain (See above). WO 96/34096 teaches multiple antibody binding domain polypeptides (*i.e.*, polypeptides comprising both a heavy chain domain *and* a light chain domain) and does not disclose single domain antibodies. Because WO 96/34096 does not teach all the elements of the claimed invention, WO 96/34096 does not anticipate the claimed invention.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

The Examiner rejected claims 1, 5, 13, 36 and 42 under 35 U.S.C. §102(e) as being anticipated by U.S. Application No. 2002/013275. According to the Examiner, US 2002/013275 teaches an anti-EGFR polypeptide such as an Fv antibody fragment comprising at least one antibody from light chain and one antibody domain from heavy chain directed against EGFR.

Applicant respectfully traverses. US 2002/013275 does not teach all the elements of the claimed invention. The single domain antibodies of the claimed invention contain only one antibody binding domain (See above). US 2002/013275 teaches multiple antibody binding domain polypeptides (*i.e.*, polypeptides comprising both a heavy chain domain *and* a light chain domain) and does not disclose single domain antibodies. Because US 2002/013275 does not teach all the elements of the claimed invention, US 2002/013275 does not anticipate the claimed invention.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

The Examiner rejected claims 1, 3, 19, 21, 23, 25, 27, 29, 31, 33 and 43-45 under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 7,300,655. According to the Examiner, US 7,300,655 teaches a bispecific antibody fusion protein comprising a single binding domain that binds to EGFR polypeptide such as an Fv of anti-EGFR and a single domain antibody that binds to serum protein such as alpha-fetoprotein wherein the antibody is produced by llamas.

Applicant respectfully traverses. US 7,300,655 does not teach all the elements of the claimed invention. The single domain antibodies of the claimed invention contain only one antibody binding domain (See above). US 7,300,655 teaches fusion proteins comprising multiple domain antibodies or polypeptides, such as Fv or scFv. These multiple domain antibodies and polypeptides comprise both a heavy chain domain *and* a light chain domain, and US 7,300,655 does not disclose single domain antibodies. Furthermore, in contrast to the assertion by the Examiner, US 7,300,655 does not teach llama derived antibodies. The llamas of US 7,300,655 (Column 30,lines 37-40) are one of the examples of domestic animals, such as horses, to which antibodies can be administered. There is no disclosure of llama derived antibodies in US 7,300,655.

Because US 7,300,655 does not teach all the elements of the claimed invention, US 7,300,655 does not anticipate the claimed invention.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. §103

The Examiner rejected claims 1 and 4-7 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 7,300,655 in view of WO 96/34096 and WO 94/04678. According to the Examiner, US 7,300,655 teaches bispecific fusion proteins antibodies that are useful for the treatment and diagnosing of tumor expressing EGFR. Further, according to the Examiner, WO96/34096 teaches an anti-EGFR polypeptide such as an Fv antibody fragment from fully-human antibody that binds specifically to EGFR comprising at least one antibody from light chain linked to one antibody domain from heavy chain directed against EGFR, and WO96/34096 teaches human antibodies against human TNF-alpha, IFN gamma receptor or TNF-alpha. In addition, according to the Examiner, WO 94/04678 teaches methods of making single domain antibodies such as VHH antibodies from camels. Finally, according to the Examiner, it would have been obvious to one of ordinary skill in the art to combine the teachings of US 7,300,655, WO 96/34096 and WO 94/04678 to arrive at the claimed invention.

Applicant respectfully traverses. The combination of US 7,300,655, WO 96/34096 and WO 94/04678 do not teach all the limitations of the claimed invention. Namely, the cited references, alone or in combination, do not disclose "a single domain antibody directed against EGFR, *wherein*

said single domain antibody inhibits and/or blocks the interaction between EGF and EGFR". The teachings of US 7,300,655 are limited to a construct comprising an anti-AFP antibody linked to a second antibody, wherein the second antibody can be directed against over 30 different proteins including EGFR. However, an anti-EGFR antibody is not actually provided, let alone any teachings pertaining to an antibody that inhibits and/or blocks the interaction between EGF and EGFR. Furthermore, the teachings of US 7,300,655 are limited to single chain antibodies comprising both a heavy chain domain and a light chain domain. The teachings of WO 96/34096 pertain to humanized antibodies. A list of over 200 antibody targets is provided (pages 13-15) and EGFR is one of the entries on this list. However, an anti-EGFR antibody is not actually provided, let alone any teachings pertaining to an antibody that inhibits and/or blocks the interaction between EGF and EGFR. WO 94/04678 pertains to methods of making single domain antibodies and WO 94/04678 remains silent on antibodies that inhibit and/or block the interaction between EGF and EGFR

Thus, US 7,300,655, WO 96/34096 and WO 94/04678 do not teach all the elements of the claimed invention. The cited references, at least therefore, do not render obvious the claimed invention.

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, the Director is hereby authorized to charge any deficiency or credit any overpayment in the fees filed, asserted to be filed or which should have been filed herewith to our Deposit Account No. 23/2825, under Docket No.: A0848.70011US00.

Respectfully submitted,
Toon Laeremans et al., Applicant(s)

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